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Efficiency of Ferrotherapy When Using Different Groups of Iron Drugs in Patients with Helicobacter Pylori

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Abstract: To date, a number of scientific studies are being conducted in the world devoted to the study of various variants of the manifestation of helicobacteriosis. Special attention should be paid to studies on the pathogenesis of iron drugs (ID) in helicobacteriosis and the role of eradication therapy in improving the effectiveness of iron therapy. Despite the fact that there are results of numerous studies confirming the role of HP in the development of ID, there are still unresolved issues related to determining the exact indications for specific therapy aimed at eradicating this infection in cases where patients with clinical and laboratory signs of ID do not have obvious symptoms damage to the gastric mucosa.

Keywords: Iron-deficiency anemia; Helicobacter pylori; iron drugs; eradication therapy.

Introduction

The prevalence of H. pylori among all segments of the population is very wide. According to the literature, more than half of people worldwide are infected with this bacterium [1, 2]. Indisputable proof of the existence of a link between H. Pylori and iron deficiency anemia (IDA) is an increase in the level of ferritin and hemoglobin after eradication therapy without additional intake of iron drugs (ID). Four meta-analyses can be found in the literature that have examined the role of H. pylori eradication therapy in reducing iron deficiency and correcting IDA. All of these studies have shown that eradication of H. pylori increases serum ferritin levels and is effective in the treatment of IDA. It has also been proven that patients with IDA who have confirmed the presence of H. Pylori have a low response to ID before H. pylori eradication [3,4,5].

Epidemiological studies in children have also shown an association between H. pylori, reduced ferritin levels, and the incidence of IDA [6]. Studies that have been conducted in both developed and developing countries have shown lower ferretin levels and a higher incidence of IDA in H. Pylori positive children [7]. The NHANES study showed that 32% of IDA cases in the US are associated with H. pylori [9]. Similar results were shown by a study of IP and H. pylori in children conducted in Turkiye [10,22,23].

To date, according to the Maastricht IV agreement, eradication of H. pylori is recommended in patients with confirmed persistence of infection and IDA after exclusion of other etiological factors [11,12,24,27]. At the same time, the role of H. Pylori in the development of IDA, the impact on resistance to treatment of the require further, deeper research.

Target. To study the effectiveness of IDA therapy with iron preparations of various groups in patients with H. Pylori.

Material and research methods. The study included 56 patients aged 18 to 40 years with moderate IDA who were laboratory confirmed to have H. pylori. The patients included 21 men and 35 women.

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Criteria for exclusion from the study:

- a history of liver and intestinal diseases that affect the absorption and metabolism of iron in the body;
- the presence of evidence of a confirmed gastric or duodenal ulcer;
- conducting earlier eradication therapy for H. pylori.

The diagnosis in patients was confirmed using traditional clinical research methods and laboratory diagnostics. In all patients included in the study, the presence of H. pylori was confirmed by the results of a urea breath test using the Helik-test system before therapy.

The study consisted of 2 stages (Fig. 1).

At the first stage, patients were divided into 2 homogeneous groups, main and comparative, 28 patients each. At the first stage, patients received ferrotherapy for 1 month without concomitant eradication therapy. Patients of the main group took trivalent ferrous iron preparations in the form of tablets of 100 mg 1 time per day. Patients of the comparative group took divalent ferrous iron preparations in the form of iron sulfate preparations, 100 mg 1 time per day.

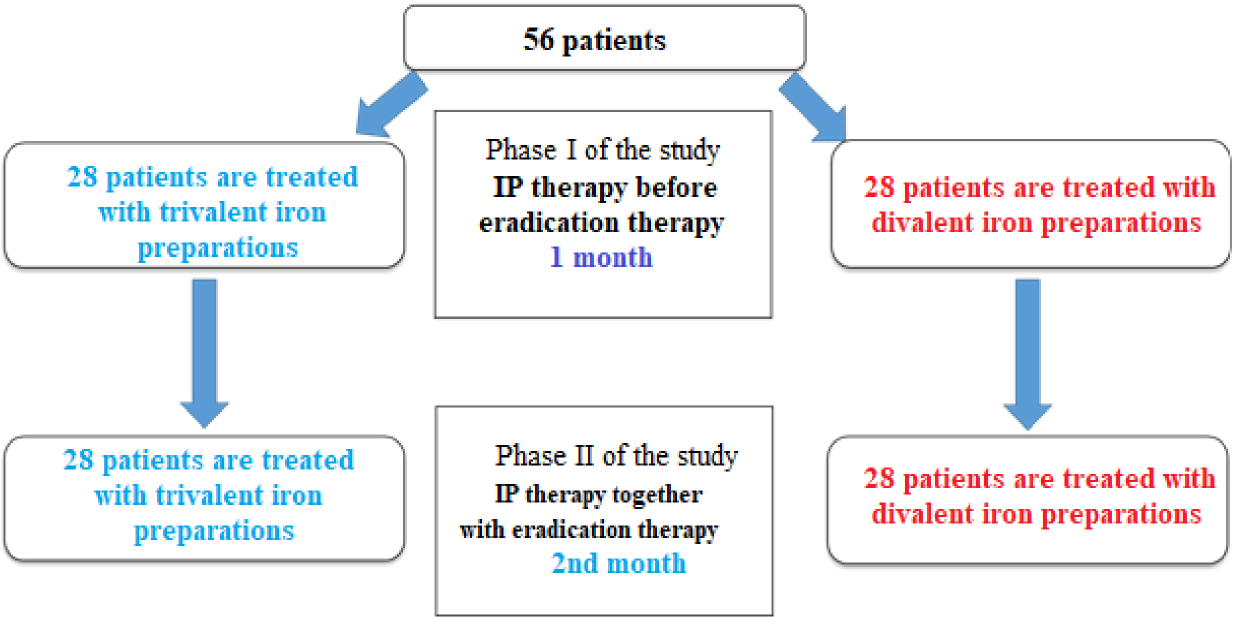


Figure 1. Study design.

At the second stage of the study, all patients, along with ferrotherapy, received eradication therapy, including amoxicillin (1000 mg 2 times a day), clarithromycin (500 mg 2 times a day) and omeprazole (20 mg 2 times a day) for 10 days (according to the recommendations of Maastricht -IV)

Evaluation of the effectiveness of IDA therapy was carried out on the basis of monitoring of hemoglobin (Hb), ferritin and serum iron levels. Statistical analysis was carried out using the standard MS Office 2019 software package using nonparametric and parametric criteria. Differences were considered significant at $p<0.05$.

Results

The results of monitoring laboratory indicators of the effectiveness of ferrotherapy at the first stage of the study are presented in Table 1. The table shows that the initial values of the average levels of hemoglobin, ferritin and serum iron did not have statistical differences in the study groups.

Data analysis by the end of the first month of treatment showed that in both study groups there was an increase in hemoglobin levels. At the same time, statistically differences in comparison with indicators before treatment were not significant due to a fairly wide spread of indicators in the sample itself. In general, it can be stated that in the main group, an increase in the average hemoglobin level by 10.7% was determined, while in the comparative group, the indicator increased by 13.8%. It should be noted that an increase in the average hemoglobin level by 10 g/l for 4 weeks, which is considered according to generally accepted standards as a criterion for the success of ferrotherapy, was achieved only in the comparison group.

The dynamics of the level of ferritin growth showed that after a monthly course of ferrotherapy in both groups, an indicator below 30 µg/l, which is considered a criterion for the effectiveness of ferrotherapy, was recorded. At the same time, in the comparative group, the average increase was also higher than in the main group. A similar trend was observed for serum iron levels (Table 1).

Table 1. Dynamics of laboratory parameters in patients in the study groups at the first stage of the study.

Index	Main group (n=28)		Comparative group (n=28)	
	before	End of 1 month	before	End of 1 month
Hemoglobin (g/l)	75.45±3.76	83.3±2.4	74.32±2.71	85.68±4.2
Ferritin (µg/l)	23.3±6.54	26.54±3.45	22.7±5.12	28.13±4.14
Serum iron (mg/l)	1.1±0.12	1.21±0.12	1.12±0.09	1.28±0.11

*-differences in comparison with indicators before treatment are statistically significant at p<0.05; ^-differences in comparison with the indicators of the comparative group are statistically significant at p<0.05;

At the second stage of the study, all patients along with ferrotherapy received a course of eradication therapy. Data analysis by the end of the second month of treatment showed that in both study groups there was a statistically significant increase in hemoglobin levels (p<0.05). At the same time, there were no statistically significant differences in the indicators by the end of 2 months of treatment in the main and comparative groups. It should be noted that in both groups, after eradication therapy, it was possible to achieve a level of hemoglobin increase of more than 10 g/l for 4 weeks, which is considered, according to generally accepted standards, a criterion for the success of ferrotherapy (Table 2).

Table 2. Dynamics of laboratory parameters in patients in the study groups at the second stage of the study.

Index	Main group (n=28)		Comparative group (n=28)	
	initially	End of 2 months	initially	End of 2 months
Hemoglobin (g/l)	83.3±2.4	98.62±2.3*	85.68±4.2	99.28±3.34*
Ferritin (µg/l)	26.54±3.45	38.25±3.11*	28.13±4.14	39.23±4.12*
Serum iron (mg/l)	1.21±0.12	1.45±0.08	1.28±0.11	1.48±0.14

*-differences in comparison with indicators before treatment are statistically significant at p<0.05; ^-differences in comparison with the indicators of the comparative group are statistically significant at p<0.05;

The dynamics of the level of ferritin growth at the second stage of the study showed that after a monthly course of ferrotherapy with eradication therapy in both groups, an indicator above 30 µg/l, which is considered a criterion for the effectiveness of ferrotherapy, was recorded. At the same time,

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there were no statistically significant differences in the indicators in the 2 studied groups. A similar trend was observed for serum iron levels.

Conclusion

The relationship between H. pylori and IDA has been convincingly proven in numerous studies. Current international and national guidelines recommend H. pylori eradication in patients with unexplained IDA, which was also confirmed by our study [13,14].

A meta-analysis including 16 different studies including a total of 956 patients showed that eradication therapy in combination with prostate therapy led to a statistically significant increase in hemoglobin levels by 1.48 times, serum iron by 1.15 times and ferritin by 1.84 times compared with ID therapy alone. All this allowed international experts studying H. pylori infection in 2010 to include IDA of unknown etiology as an additional indication for eradication therapy [30,31,32].

The results of the analysis of 17 thousand cases showed the prevalence of IDA in 5.5% of patients with H. pylori infection compared with 5.2% in the group with negative results of the study for the bacterium. The relative risk of IDA in patients with H. pylori was 1.19. There was also an increased risk of developing moderate to severe IDA in patients with H. pylori, in whom the relative risk ratio was 1.39 [18,19,33].

The results of this study allow us to state that the presence of H. pylori had a more pronounced effect on the degree of absorption of the ID in patients receiving trivalent ferric iron preparations. At the same time, it was found that after the eradication therapy in patients taking Fe (III) preparations, a more pronounced increase in the therapeutic effect was observed, expressed in a more significant and significant increase in the main laboratory parameters in the form of hemoglobin and ferritin levels.

The results of this study are consistent with the results of foreign studies, which showed that the H. pylori bacterium is able to secrete special chelate complexes that have an affinity for ferric iron, which helps them absorb iron for their life. It is known that this microorganism synthesizes proteins that contain ferric iron, that is, they directly need it [18,19,20].

Thus, the study showed that H. pylori infection is a significant factor influencing the therapeutic efficacy of ferric iron preparations. This fact must be taken into account when prescribing this group of drugs for ferrotherapy and when confirming the presence of H. pylori, it is advisable to conduct concomitant eradication therapy.

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